

REMARKS

Claim Amendments:

Claims 1-5, 12-15, 17-21 and 23-25 have been canceled. Claims 6, 8, 16, 22 and 26-28 have been amended. New claims 35-51 have been added. Claims 6, 8, 16 and 22 have been amended to depend from claim 26. Claim 22 has also been amended to correct a typographical error. Claim 26 has been amended to clarify the claimed invention. Support for this amendment may be found, for example, at page 22, lines 8-15 of the specification. Claims 27 and 28 have been rewritten in independent form, incorporating all the limitations of claim 26. New claims 35-51 generally correspond to claims 6, 8-11, 16, 22, 29 and 30, but depend from newly independent claims 27 and 28.

No new matter has been added by these amendments. The Examiner is requested to enter these amendments.

New Matter Objection and Rejection:

The Examiner's objection to claim 26 under 35 U.S.C. 132 and rejection of claims 26-30 under 35 U.S.C. 112, first paragraph as containing new matter are respectfully traversed. In addition to the support contained in original claim 26, the specification provides additional disclosure of each step of this claim. For example, at page 22, lines 8-15 the specification describes preventing a neoplasm from developing drug resistance. This paragraph describes the use of reovirus to treat a subject "at the onset of the course of chemotherapy such that all cells are killed or inhibited, including drug resistant cells." Clearly a "course of chemotherapy" given to a subject where "all the cells" includes drug sensitive cells as well as drug resistant cells identifies a subject including neoplastic cells susceptible to a chemotherapeutic agent. Accordingly, Applicants submit that claims 26-30 do not contain new matter.

Withdrawal of the objection and rejection is requested.

Double Patenting Rejections:

The Examiner's rejection of claims 1-6 and 8-25 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1 and 28 of U.S. Patent No. 6,565,831 B1) in view of Smith is respectfully traversed in view of the above amendments, in which each of these claims was either canceled or amended to depend from non-rejected claim 26.

The Examiner's rejection of claims 1-6 and 8-25 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1, 3-8, 13-20 and 24-34 of U.S. Patent No. 6,136,307 A) in view of Smith is respectfully traversed in view of the above amendments, in which each of these claims was either canceled or amended to depend from non-rejected claim 26.

Rejections Under 35 U.S.C. 103:

The Examiner's rejection of claims 1-25 under 35 U.S.C. 103 (a) as unpatentable over U.S. Patent No. 6,136,307 A in view of Smith is respectfully traversed in view of the above amendments, in which each of these claims was either canceled or amended to depend from non-rejected claim 26.

The Examiner's rejection of claims 1-25 under 35 U.S.C. 103 (a) as unpatentable over WO 00/50051 A2 in view of Smith is respectfully traversed in view of the above amendments, in which each of these claims was either canceled or amended to depend from non-rejected claim 26.

The Examiner's rejection of claims 1-25 under 35 U.S.C. 103 (a) as unpatentable over Smith is respectfully traversed in view of the above amendments, in which each of these claims was either canceled or amended to depend from non-rejected claim 26.

The Examiner's rejection of claims 1-25 under 35 U.S.C. 103 (a) as unpatentable over Mercer University in view of Smith is respectfully traversed in view of the above amendments, in which each of these claims was either canceled or amended to depend from non-rejected claim 26.

Withdrawal of the rejections is requested.

Rejection Under 35 U.S.C. 102:

The Examiner's rejection of claims 1, 4, 8, 12, 17, 19, 20, 22 and 26 under 35 U.S.C. 102 (b) as unpatentable over Williams et al. in view of Liu and Smith is respectfully traversed. The rejection of claims 1, 4, 12, 17, 19 and 20 is moot, as these claims have been canceled. Claims 8 and 22 have been amended to depend from claim 26. Applicants submit that the Examiner has not made a proper rejection under 35 U.S.C. 102(b), as the cited reference does not disclose each and every limitation of the claimed invention.¹

As an initial matter, Williams et al. disclose ex vivo treatment of L1210 leukemia cells with BCNU and, subsequently, ex vivo treatment of the BCNU-treated cells with reovirus. These treated cells are then injected into mice. In contrast, the claimed invention involves administration of reovirus and a chemotherapeutic agent *to a subject* to prevent the development of drug resistance. This is neither disclosed nor suggested by Williams et al. Neither do Williams et al. teach or suggest that reovirus may be used to prevent the development of drug resistance as in the claimed invention.

In addition, Applicants disagree that Liu (abstract) discloses that leukemia cell line L1210 is ras-activated. Liu merely discloses that a particular cis-platinum resistant strain of this cell line showed ras oncogene amplification. In contrast, the Williams et al. reference used a standard L1210 cell line. It is known that cisplatin-resistant neoplastic cells have increased expression of ras. (See, e.g., Aoki et al., "Cisplatin activates survival signals in UM-SCC-23 squamous cell carcinoma and these signal pathways are amplified in cisplatin-resistant squamous cell carcinoma," *Onc. Rep.*, 11:375-379 (2004); copy enclosed.) Thus, Liu's disclosure of a ras-activated cis-platinum resistant L1210 cell line in no way teaches or suggests that the standard L1210 line of Williams et al. was ras-activated. Further, like Williams et al., Liu does not teach or suggest the administration of reovirus and a chemotherapeutic agent *to a subject* to prevent the

¹ Applicants note that paragraph 38. of the office action explicitly raises a rejection of these claims on the grounds of obviousness, not anticipation. In view of this paragraph, this response also addresses why the presently claimed invention is patentable, as neither anticipated nor obviated, over the cited references.

development of drug resistance, as in the claimed invention. In fact, neither Williams et al. nor Liu address the prevention of the development of drug resistance in a subject at all.

Similarly, Smith et al. do not cure the deficiencies of Williams et al. and Liu. The paragraph on page 321 of Smith et al. cited by the Examiner only refers to adenovirus and HSV, not reovirus; clearly it cannot be used in support of an anticipation rejection of the present claims. Further, this paragraph only describes the effect of combination therapy on anticancer efficacy – there is no mention of prevention of the development of drug resistance at all. While the paragraph on page 319 cited by the Examiner does relate to the use of reovirus in combination with chemotherapy, it also fails to describe or address in any way the prevention of the development of drug resistance.

Withdrawal of the rejection is requested.

Conclusions:

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested. Allowance of the claims of this application at an early date is earnestly solicited.

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Enclosed is a \$510.00 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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